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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/842,637	04/27/2001	Anthony Robert Milnes Coates	Q-64007	9237

7590 01/09/2004

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EXAMINER	
MARX, IRENE	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 01/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/842,637	COATES ET AL.	
	Examiner	Art Unit	
	Irene Marx	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-7,9 and 10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7 and 9-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/25/03 has been entered.

Claims 2-7 and 9-10 are being considered on the merits

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-7 and 9-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is confusing in that there is no clear indication that the "test compound" and the "antibiotic" are different compounds. Moreover, there is no clear nexus between the growth of an "antibiotic sensitive" bacterial strain to stationary phase, the obtaining of a dormant culture and the treatment with "at least one antibiotic at a concentration and for a time sufficient to kill growing bacteria". Not all antibiotics selectively kill growing bacteria only. Also, there is no claim designated indication regarding the protocol for selection of a phenotypically antibiotic-resistant subpopulation. The resistance of the bacterial strains recited in dependent claims appears to be to one specific antibiotic, rather than "at least one antibiotic" as claim designated. In addition, it cannot be concluded from the process steps as outlined that resistance is to all antibiotics, as implied. In addition the determination of "exhibits any antibacterial activity" is uncertain, since the concentration of the test compound is not set forth. Moreover, there is no indication of what constitutes this activity. It is slowing of growth for a few minutes, slowing of growth for a few hours, or is it killing? Any compound, including a nutrient such as glucose can be shown to have "antibacterial activity", i.e., have at least some toxicity if provided at certain concentrations.

In claim 9, the step of "assaying" does not set forth with sufficient particularity how "antibacterial" activity is assessed, i.e., how the assay is done and scored and the concentration of the test compound at which the "any" antibacterial activity has to be exhibited.

Claims 2, 5, and 6 fail to find proper antecedent basis in claim 9 for "said antibiotic". The language of claim 9 is "at least one antibiotic".

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3-4, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Entenza *et al.* I (1996) or Entenza et al. *II (1994).*

The claims are directed to a process of identifying whether a test compound has any antibacterial activity against dormant bacteria wherein resistant bacteria are produced by treating stationary cultures with at least one antibiotic to select for resistant bacteria.

Entenza *et al.* I or II disclose a process of identifying whether a test compound has any antibacterial activity against dormant bacteria wherein resistant bacteria are produced by treating stationary cultures with at least one antibiotic to select for resistant bacteria. See, e.g., Materials and methods, page 71, col. 2, respectively, page 101, Materials and Methods.

Claims 3-4, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Boswell *et al.*.

The claims are directed to a process of identifying whether a test compound has any antibacterial activity against dormant bacteria wherein resistant bacteria are produced by treating stationary cultures with at least one antibiotic to select for resistant bacteria.

Boswell *et al.* disclose a process of identifying whether a test compound has any antibacterial activity against dormant bacteria wherein resistant bacteria are produced by treating stationary cultures with at least one antibiotic to select for resistant bacteria. See, e.g., Materials and Methods, and Results, pages 30-31.

Claims 3-4, and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Tuomanen *et al.*.

The claims are directed to a process of identifying whether a test compound has any antibacterial activity against dormant bacteria wherein resistant bacteria are produced by treating stationary cultures with at least one antibiotic to select for resistant bacteria.

Tuomanen *et al.* disclose a process of identifying whether a test compound has any antibacterial activity against dormant bacteria wherein resistant bacteria are produced by treating stationary cultures with at least one antibiotic to select for resistant bacteria. See, e.g., page 107

Claims 2-4, 6-7 and 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Entenza *et al.* I (1996) or Entenza et al. *II (1994)* or Boswell *et al.* or Tuomanen *et al.* taken with Shomura *et al.* and Barth for the reasons as stated in the last Office action and the further reasons below.

The claims are directed to a process of identifying whether a test compound has any antibacterial activity against bacteria wherein resistant bacteria are produced by treating stationary cultures with at least one antibiotic to select for resistant bacteria.

Entenza *et al.* I (1996), Entenza et al. *II (1994)*, Boswell *et al.*, Tuomanen *et al.* are discussed supra.

The references differ from the claimed invention in that *E. coli* resistant to kanamycin and *S. aureus* resistant to ampicillin are not specifically disclosed. However, Shomura *et al.* disclose a screening test for antimicrobial agents effective against resistant bacteria wherein kanamycin resistant *E. coli* are taught (See, e.g., col. 4, lines 35-38) and Barth disclose a screening test for antimicrobial agents effective against resistant bacteria wherein ampicillin resistant *S. aureus* are disclosed. (See, e.g., col. 14, lines 5-8).

With respect to the "amplification" process of claim 10, Shomura *et al.* provide guidelines about maximizing the producing of the compound of interest, which is deemed to constitute "amplification" as claimed. (See, e.g., Examples 1 and 2).

One of ordinary skill in the art would have had a reasonable expectation of success in applying the screening tests taught by Entenza *et al.* I (1996*)* or Entenza et al. *II (1994)* or Boswell *et al.* or Tuomanen *et al.* to a variety of resistant bacteria produced according to the methods disclosed therein or to further resistant bacteria as disclosed by Shomura and Barth, such as kanamycin-resistant *E. coli.* or ampicillin resistant *S. aureus.*

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process of Entenza *et al.* I (1996*)* or Entenza et al. *II (1994)* or Boswell *et al.* or Tuomanen *et al.* by assessing the effectiveness of antimicrobial agents on a large variety of bacteria wherein resistance is induced by the methods therein, because one of ordinary skill in the art would reasonably have expected that the techniques used by of Entenza *et al.* I (1996*)* or Entenza et al. *II (1994)* or Boswell *et al.* or Tuomanen *et al.* would be effective to produce similar resistance to the same or other antibiotics in further bacterial strains, including kanamycin resistance in *E. coli* as suggested by the teachings of Shomura *et al.* and ampicillin resistance in *S. aureus* as suggested by the teachings of Barth for the expected benefit of obtaining and testing effective chemotherapeutic agents and thus increasing the success and efficiency of the treatment dangerous bacterial infections caused by antibiotic resistant bacteria in susceptible individuals to avoid bacteremia or other complications.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Entenza *et al.* I (1996*)* or Entenza et al. *II (1994)* or Boswell *et al.* or Tuomanen *et al.* taken with Shomura *et al.* and Barth taken with Shomura *et al.* and Barth as applied to claims 2-4, 6-7 and 9-10 above, and further in view of Murray *et al.* and *The Merck Index.*

The references are discussed above.

The invention as claimed differs from the references in that rifampicin resistant *M. tuberculosis* is not disclosed. However, Murray *et al.* adequately demonstrate that resistance to rifampicin in *M. tuberculosis* is recognized in the art. (See, e.g., page 428). Also *The Merck Index* discloses that rifampin and rifampicin are one and the same (See, e.g., item 8382). One of ordinary skill in the art would reasonably have expected that the techniques used by of Entenza *et al.* I (1996*)* or Entenza et al. *II (1994)* or Boswell *et al.* or Tuomanen *et al.* would be effective

to produce similar resistance in other bacterial strains, including resistance to rifampicin in *M. tuberculosis* as suggested by Murray *et al.*.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the process of Entenza *et al.* I (1996*)* or Entenza et al. *II (1994)* or Boswell *et al.* or Tuomanen *et al.* by assessing the effectiveness of antimicrobial agents on a large variety of bacteria wherein resistance is induced by the methods therein and including kanamycin resistance in *E. coli* as suggested by the teachings of Shomura *et al.* or ampicillin resistance in *S. aureus* as suggested by the teachings of Barth or rifampicin resistance in *Mycobacterium tuberculosis,* as suggested by the teachings of Murray *et al.* for the expected benefit of identifying effective chemotherapeutic agents and thus increasing the success and efficiency in the treatment of tuberculosis, a dangerous and increasingly prevalent bacterial infection caused more and more by antibiotic resistant *Mycobacterium tuberculosis* in susceptible individuals.

Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

Applicants' arguments are moot in view of the new grounds of rejection.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Irene Marx whose telephone number is 703-308-2922. The examiner can normally be reached on M-F (6:30-3:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 703-308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0926.

Irene Marx
Primary Examiner
Art Unit 1651